

10/646266

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* * * * * Welcome to STN International * * * * *

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NEWS 6 DEC 01 LISA now available on STN
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NEWS 10 DEC 17 COMPUAB reloaded; updating to resume; current-awareness
alerts (SDIs) affected
NEWS 11 DEC 17 SOLIDSTATE reloaded; updating to resume; current-awareness
alerts (SDIs) affected
NEWS 12 DEC 17 CERAB reloaded; updating to resume; current-awareness
alerts (SDIs) affected
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NEWS 15 DEC 30 CAPLUS - PATENT COVERAGE EXPANDED
NEWS 16 JAN 03 No connect-hour charges in EPFULL during January and
February 2005
NEWS 17 JAN 26 CA/CAPLUS - Expanded patent coverage to include the Russian
Agency for Patents and Trademarks (ROSPATENT)
NEWS 18 FEB 10 STN Patent Forums to be held in March 2005

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 16:17:39 ON 10 FEB 2005

| | |
|------------|---------|
| SINCE FILE | TOTAL |
| ENTRY | SESSION |
| 0.21 | 0.21 |

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

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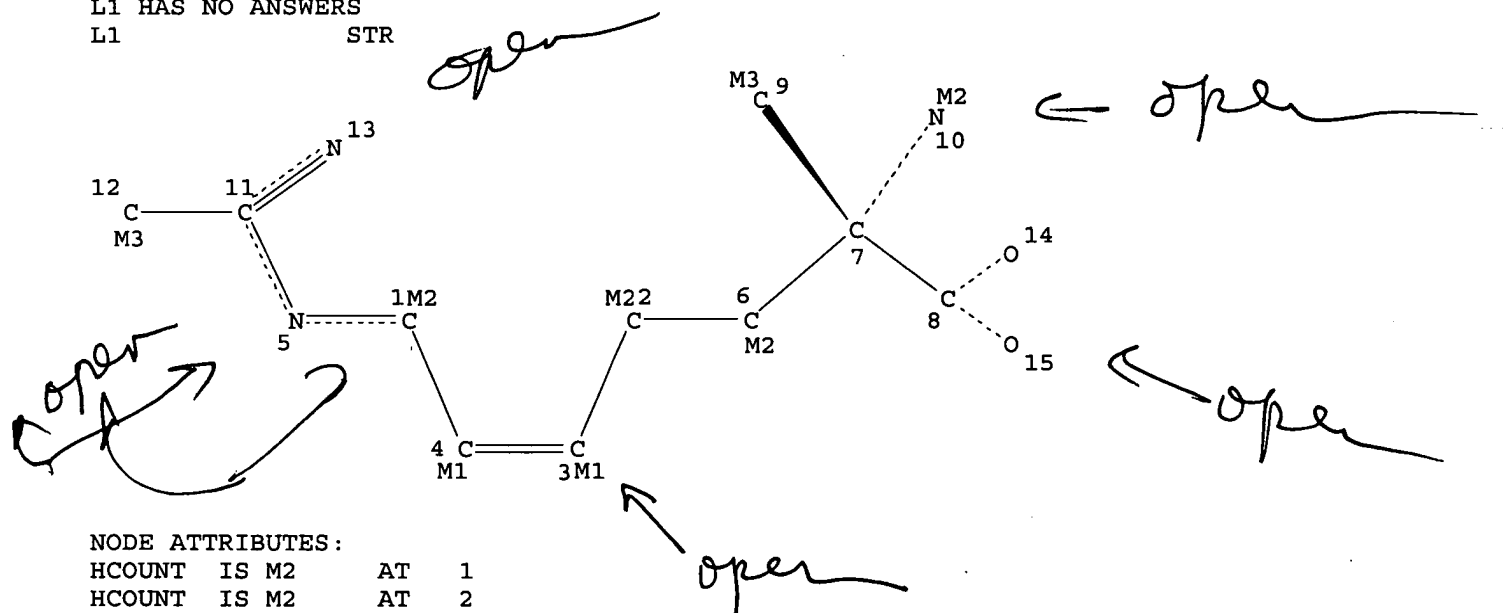
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1                                STR
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NODE ATTRIBUTES:
HCOUNT  IS M2      AT  1
HCOUNT  IS M2      AT  2
HCOUNT  IS M1      AT  3
HCOUNT  IS M1      AT  4
HCOUNT  IS M2      AT  6

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10/646266

HCOUNT IS M3 AT 9
HCOUNT IS M2 AT 10
HCOUNT IS M3 AT 12
NSPEC IS C AT 1
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DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES:
STEREO DEFAULT RELATIVE
NUMBER OF CHIRAL CENTERS IS 1
SS1 REL 7

=> s l1 full
FULL SEARCH INITIATED 16:18:19 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 520 TO ITERATE

100.0% PROCESSED 520 ITERATIONS 10 ANSWERS
SEARCH TIME: 00.00.01

L2 10 SEA SSS FUL L1

| => file caplus | SINCE FILE | TOTAL |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | ENTRY | SESSION |
| FULL ESTIMATED COST | 161.33 | 161.54 |

FILE 'CAPLUS' ENTERED AT 16:18:37 ON 10 FEB 2005
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10/646266

FILE COVERS 1907 - 10 Feb 2005 VOL 142 ISS 7
FILE LAST UPDATED: 9 Feb 2005 (20050209/ED)

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=> s 12

L3 9 L2

=> d bib abs hitstr 1-9 13

L3 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:780756 CAPLUS

DN 141:296928

TI Exchanger for selectively removing counterions from compounds and
compounds derived from the methods for pharmaceutical applications

IN Moore, Christine June

PA Pharmacia Corporation, USA

SO PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004081073 | A2 | 20040923 | WO 2004-IB529 | 20040223 |
| | WO 2004081073 | A3 | 20041111 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2004225150 | A1 | 20041111 | US 2004-797350 | 20040310 |
| PRAI | US 2003-453798P | P | 20030311 | | |

AB Compds. derived such as S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-
cysteine (I) zwitterion with 0-2 molar equivalents of hydrochloride are
also disclosed. The chloride removal process was run in batch, but it
could easily be run in a plant setting by recirculating the I
dihydrochloride solution over an anion exchange resin column or an anion
exchange membrane such as Amberlite 400. If the pH is inadvertently
raised beyond the desired range, it may easily be adjusted back by adding
an appropriate amount of HCl.

IT 404385-39-3

RL: PEP (Physical, engineering or chemical process); PYP (Physical
process); PROC (Process)

(exchanger for selectively removing counterions from amino acid compds.
suitable for pharmaceutical applications)

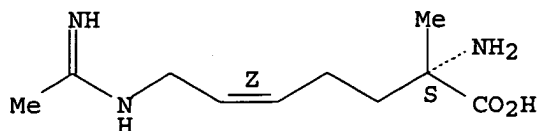
RN 404385-39-3 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-,
dihydrochloride, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

NP 44



● 2 HCl

L3 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:182830 CAPLUS

DN 140:223311

TI Crystalline solid form of (2S,5Z)-2-amino-7-(ethanimidoamino)-2-methylhept-5-enoic acid

IN Hallinan, Ann E.

PA Pharmacia Corporation, USA

SO PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------|---|------|----------|-----------------|----------|
| PI | WO 2004018412 | A1 | 20040304 | WO 2003-US26347 | 20030822 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2004132822 | A1 | 20040708 | US 2003-646266 | 20030822 |
| X PRAI | US 2002-405526P | P | 20020823 | | |

AB (2S,5Z)-2-amino-7-(ethanimidoamino)-2-methylhept-5-enoic acid (I) is crystallized as an anhydrous, stoichiometric 1.5 HCl salt and a scaleable crystallization

method is disclosed. The salt form was characterized and the absolute configuration of the chiral center was confirmed as I was high melting and appears acceptably nonhygroscopic for use in a pharmaceutical composition. Thus, I was prepared in a series of steps starting from 5,5-dihydro-2-pyrone and (Z)-5-tert-butyltrimethylsilyloxy-2-penten-1-ol.

IT 404385-91-7P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(crystalline solid form of amino(ethanimidoamino)methylheptenoic acid)

RN 404385-91-7 CAPLUS

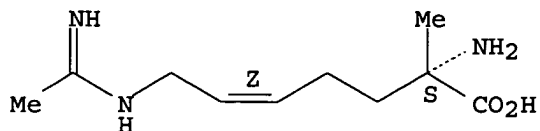
CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2S,5Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

Same Inventor Work

10/646266



IT 404385-39-3P 666748-92-1P 666748-93-2P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

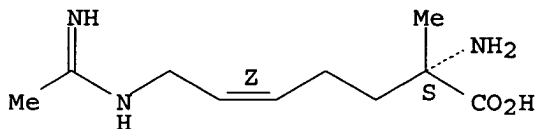
BIOL (Biological study); PREP (Preparation); USES (Uses)

(crystalline solid form of amino(ethanimidoethylamino)methylheptenoic acid)

RN 404385-39-3 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

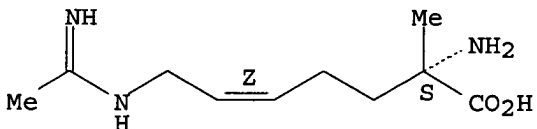


● 2 HCl

RN 666748-92-1 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, hydrochloride, hydrate (2:5:4), (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



● 5/2 HCl

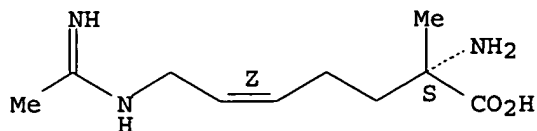
● 2 H₂O

RN 666748-93-2 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, hydrochloride (2:3), (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

10/646266



● 3/2 HCl

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:120714 CAPLUS
DN 140:164231
TI Preparation of 2,7-diamino-5-heptenoic acid derivatives for the treatment
and prevention of gastrointestinal conditions
IN Manning, Pamela T.; Connor, Jane R.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 215 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | WO 2004012726 | A2 | 20040212 | WO 2003-US23324 | 20030725 |
| | WO 2004012726 | A3 | 20040603 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | US 2004127569 | A1 | 20040701 | US 2003-626941 | 20030725 |
| PRAI | US 2002-400660P | P | 20020802 | | |

OS MARPAT 140:164231

AB The invention describes therapeutic methods for the prevention and treatment of conditions and diseases of the gastrointestinal tract involving an overprodn. of nitric oxide by inducible nitric oxide synthase (iNOS) by administering a therapeutically effective amount of a selective inhibitor of iNOS. The methods also include the use of selective inhibitors of iNOS in combination with other therapeutic agents, including antimicrobial agents and antisecretory agents. 2,7-Diamino-5-heptenoic acid derivs. R7N:CM₂NHCH₂CR₁:CR₂CH₂CH₂CH(NH₂)C(O)J [R₁, R₂ = H, halo, alkyl, haloalkyl (at least one of R₁ or R₂ contains halogen); R₇ = H, OH; J = OH, alkoxy, NR₃R₄, where R₃ = H, alkyl, alkenyl, alkynyl and R₄ = H, (un)substituted heterocyclyl] or their pharmaceutically-acceptable salts are among the compds. claimed. Thus, (2S,5E)-2-amino-6-fluoro-7-[(1-iminoethyl)amino]-5-heptenoic acid dihydrochloride was prepared by a multistep procedure starting from L-glutamic acid and showed IC₅₀ values 0.36, 68, 3.6, and 0.1 μM in hiNOS, hecNOS, hncNOS, and human cartilage assays, resp.

IT 404385-53-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

NPA

10/646266

(Uses)

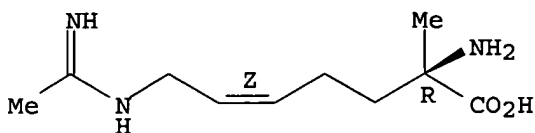
(preparation of diaminoheptenoic acid derivs. for treatment and prevention of gastrointestinal conditions)

RN 404385-53-1 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2R,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



● 2 HCl

Handwritten signature: # Compound

L3 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:931225 CAPLUS

DN 140:5301

TI Preparation of amino acid derivatives and methods for the treatment of respiratory diseases and conditions using a selective inos inhibitor

IN Manning, Pamela T.

PA Pharmacia Corporation, USA

SO PCT Int. Appl., 221 pp.

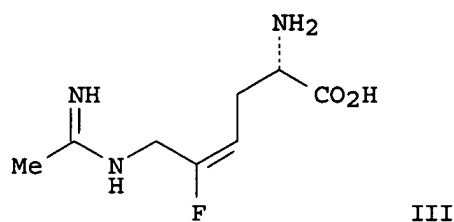
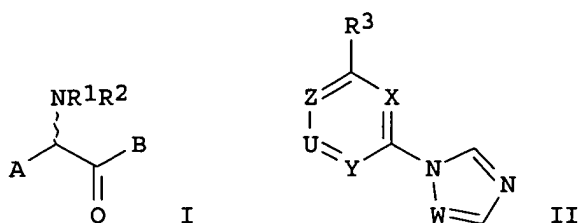
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | WO 2003097163 | A2 | 20031127 | WO 2003-US15369 | 20030516 |
| | WO 2003097163 | A3 | 20041021 | | |
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| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | US 2004077639 | A1 | 20040422 | US 2003-439669 | 20030516 |
| PRAI | US 2002-381054P | P | 20020516 | | |
| OS | MARPAT 140:5301 | | | | |
| GI | | | | | |



≠ Compound

AB Compds. I [A = (un)substituted-iminoalkylaminoalkenyl, -iminoalkylaminoalkynyl, -aminoalkylaminoalkylthioalkyl, etc.; B = OH, alkoxy, etc.; R1 and R2, independently = H, alkyl, alkenyl aryl, etc.] and II [R3 = (un)substituted-alkylthio, -alkyloxy, -alkylcarbocyclalkyl, -nitrogen heterocycle, etc.; X, Y and Z are independently N or substituted C; U = N or substituted C with provision that U is N only when X is N and Z and Y are substituted C; W = N or CH] as well as their pharmaceutically acceptable salts are prepared and claimed as selective inhibitors of inducible nitric oxide synthase. Thus, e.g., III was prepared in eight steps from L-glutamic acid via intermediate coupling of N-Boc protected Me 5-oxopentanoate (preparation given) with tri-Et 2-fluorophosphonoacetate which was followed by hydrolysis, substitution with 3-methyl-1,2,4-oxadiazolin-5-one, acid catalyzed ring cleavage to the iminoethylamine derivative and subsequent deprotection steps. In citrulline assays for human inducible nitric oxide synthesis, I possessed IC50 values of 0.36-197 μ M. Therapeutic methods for the prevention and treatment of respiratory diseases or conditions are described, the methods including administering to a subject in need thereof a respiratory disease or condition effective amount of a selective inhibitor of inducible nitric oxide synthase.

IT 404385-39-3P 404385-53-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

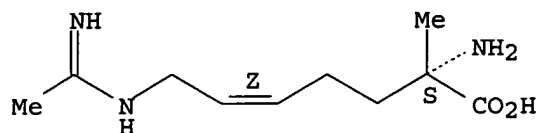
(drug candidates; preparation of amino acid derivs. and methods for the treatment of respiratory diseases and conditions using a selective inducible nitric oxide synthase inhibitor)

RN 404385-39-3 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

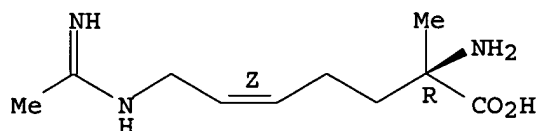
10/646266



● 2 HCl

RN 404385-53-1 CAPLUS
CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-,
dihydrochloride, (2R,5Z)- (9CI) (CA INDEX NAME)

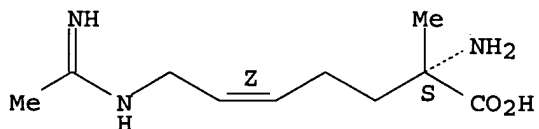
Absolute stereochemistry.
Double bond geometry as shown.



● 2 HCl

IT 404385-91-7P 505098-89-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(intermediate; preparation of amino acid derivs. and methods for the
treatment of respiratory diseases and conditions using a selective
inducible nitric oxide synthase inhibitor)
RN 404385-91-7 CAPLUS
CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2S,5Z)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



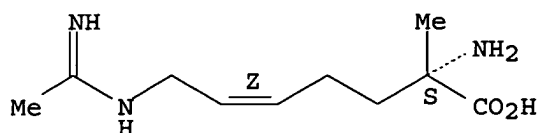
RN 505098-89-5 CAPLUS
CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2S,5Z)-,
bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 404385-91-7
CMF C10 H19 N3 O2

Absolute stereochemistry.
Double bond geometry as shown.

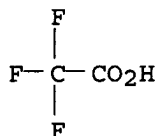
10/646266



CM 2

CRN 76-05-1

CMF C2 H F3 O2



L3 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:931174 CAPLUS
DN 140:16957
TI Preparation of amino acid derivatives in methods for the treatment of
respiratory diseases and conditions with a selective iNOS inhibitor and a
PDE inhibitor
IN Manning, Pamela T.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 245 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|----------|
| PI | WO 2003097050 | A2 | 20031127 | WO 2003-US15464 | 20030516 |
| | WO 2003097050 | A3 | 20040617 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---------------|----|----------|----------------|----------|
| US 2004087653 | A1 | 20040506 | US 2003-439679 | 20030516 |
|---------------|----|----------|----------------|----------|

PRAI US 2002-381056P P 20020516

OS MARPAT 140:16957

AB The invention claims a combination of an iNOS blocker and a
phosphodiesterase (PDE) inhibitor or their pharmaceutically-acceptable
salts or prodrugs for the prevention and treatment of respiratory diseases
or conditions. The iNOS inhibitors include amino acids
HN:CMenHCH2CHRSCH2CH(NH2)CO2H (R = alkyl, cycloalkyl, hydroxyalkyl, or
haloalkyl). Thus, 2S-amino-6-[(1-iminoethyl)amino]-N-(1H-tetrazol-5-
yl)hexanamide dihydrochloride (NN) was prepared and shown to be a more
potent i-NOS inhibitor (IC50 = 21.4 μ M) than 2S-amino-6-[(1-
iminoethyl)amino]hexanamide (NIL amide) or NIL dimethylamide. NN is a
nicely crystalline product, in contrast to NIL which is a glass and thus

10/646266

difficult to handle.

IT 404385-39-3P 404385-53-1P

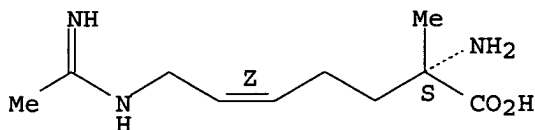
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid derivs. in methods for treatment of respiratory diseases with selective iNOS inhibitor and PDE inhibitor)

RN 404385-39-3 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



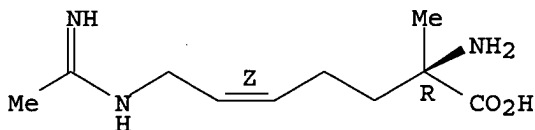
≠ Salt

● 2 HCl

RN 404385-53-1 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2R,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



≠ Salt

● 2 HCl

IT 505098-89-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amino acid derivs. in methods for treatment of respiratory diseases with selective iNOS inhibitor and PDE inhibitor)

RN 505098-89-5 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2S,5Z)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

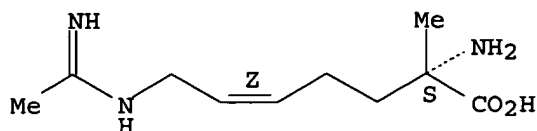
CM 1

CRN 404385-91-7

CMF C10 H19 N3 O2

Absolute stereochemistry.
Double bond geometry as shown.

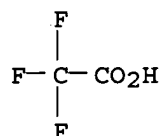
10/646266



CM 2

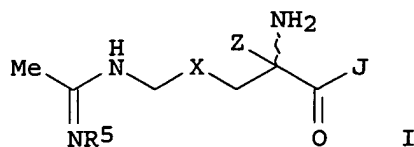
CRN 76-05-1

CMF C2 H F3 O2



L3 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:261685 CAPLUS
DN 138:287966
TI Preparation of amino acid derivatives as selective nitric oxide synthase
inhibitors for ophthalmol. treatment
IN Manning, Pamela T.; Connor, Jane R.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2003026668 | A1 | 20030403 | WO 2002-US30213 | 20020924 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2003109522 | A1 | 20030612 | US 2001-961816 | 20010924 |
| | EP 1429777 | A1 | 20040623 | EP 2002-761803 | 20020924 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | BR 2002012991 | A | 20040817 | BR 2002-12991 | 20020924 |
| PRAI | US 2001-961816 | A | 20010924 | | |
| | WO 2002-US30213 | W | 20020924 | | |
| OS | MARPAT 138:287966 | | | | |
| GI | | | | | |



AB The acetamidino amino acid derivs. I [R5 = H, or OH; X = CR1:CR2CH2, CR1:CR2, CH2CR1:CR2, C.tplbond.C, CH2C.tplbond.C, C.tplbond.CCH2; R1, R2 = H, halo, alkyl, or haloalkyl; with the proviso that at list one of R1 or R2 contains halo; Z = H, (un)substituted alkyl, alkoxy, or halo; J = H, OH, alkoxy, NR3R4; R3 = H, alkyl, alkenyl, alkynyl; R4 = H, or (un)substituted heterocyclyl] and related 7-iminoheptahydro-2-azepinyl derivs. were prepared as selective nitric oxide synthase inhibitors for ophthalmol. treatment. Thus, (2S,5E)-2-amino-6-fluoro-7-[(1-iminoethyl)amino]-5-heptenoic acid dihydrochloride prepared by a multistep procedure starting from L-glutamic acid inhibited the LPS-induced increase in plasma nitrite/nitrate levels with an observed ED50 value of <0.1 mg/kg demonstrating the ability to inhibit inducible nitric oxide synthase activity in vivo.

IT 404385-39-3P 404385-53-1P

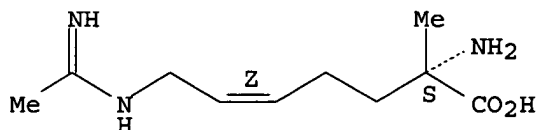
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid derivs. as selective nitric oxide synthase inhibitors for ophthalmol. treatment)

RN 404385-39-3 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



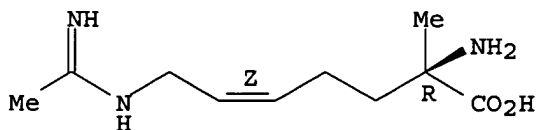
● 2 HCl

Comp

RN 404385-53-1 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2R,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



● 2 HCl

Comp.

10/646266

IT 505098-89-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amino acid derivs. as selective nitric oxide synthase inhibitors for ophthalmol. treatment)

RN 505098-89-5 CAPLUS

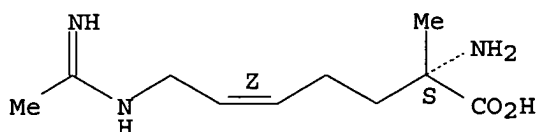
CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2S,5Z)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 404385-91-7

CMF C10 H19 N3 O2

Absolute stereochemistry.
Double bond geometry as shown.

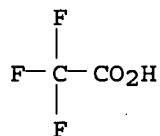


f Comp.

CM 2

CRN 76-05-1

CMF C2 H F3 O2



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:261658 CAPLUS

DN 138:287965

TI Preparation of amino acid derivatives as selective nitric oxide synthase inhibitors for neuroprotective treatment

IN Manning, Pamela T.; Connor, Jane R.

PA Pharmacia Corporation, USA

SO PCT Int. Appl., 185 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| PI | WO 2003026638 | A1 | 20030403 | WO 2002-US30214 | 20020924 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |

10/646266

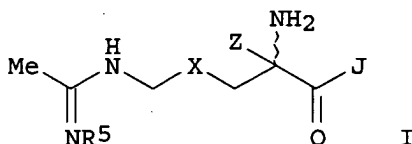
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003119826 A1 20030626 US 2001-961521 20010924
EP 1429752 A1 20040623 EP 2002-761804 20020924

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2001-961521 A 20010924
WO 2002-US30214 W 20020924

OS MARPAT 138:287965
GI



AB The acetamidino amino acid derivs. I [R5 = H, or OH; X = CR1:CR2CH2, CR1:CR2, CH2CR1:CR2, C.tplbond.C, CH2C.tplbond.C, C.tplbond.CCH2; R1, R2 = H, halo, alkyl, or haloalkyl; with the proviso that at least one of R1 or R2 contains halo; Z = H, (un)substituted alkyl, alkoxy, or halo; J = H, OH, alkoxy, NR3R4; R3 = H, alkyl, alkenyl, alkynyl; R4 = H, or (un)substituted heterocyclyl] and related 7-iminoheptahydro-2-azepinyl derivs. were prepared as selective nitric oxide synthase inhibitors for the prevention and treatment of neurodegenerative conditions. Thus, (2S,5E)-2-amino-6-fluoro-7-[(1-iminoethyl)amino]-5-heptenoic acid dihydrochloride prepared by a multistep procedure starting from L-glutamic acid inhibited the LPS-induced increase in plasma nitrite/nitrate levels with an observed ED50 value of <0.1 mg/kg demonstrating the ability to inhibit inducible nitric oxide synthase activity in vivo.

IT 404385-39-3P 404385-53-1P

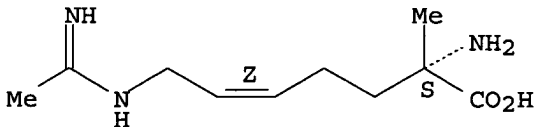
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid derivs. as selective nitric oxide synthase inhibitors for treatment of neurodegenerative conditions)

RN 404385-39-3 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



Comp.

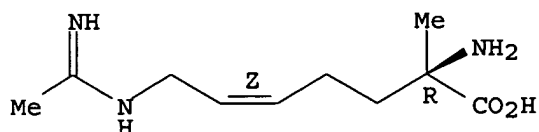
● 2 HCl

RN 404385-53-1 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2R,5Z)- (9CI) (CA INDEX NAME)

10/646266

Absolute stereochemistry.
Double bond geometry as shown.



≠ Comp.

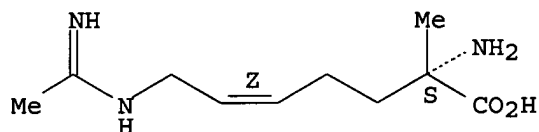
● 2 HCl

IT 505098-89-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid derivs. as selective nitric oxide synthase inhibitors for treatment of neurodegenerative conditions)
RN 505098-89-5 CAPLUS
CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2S,5Z)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 404385-91-7
CMF C10 H19 N3 O2

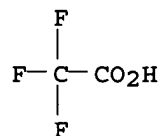
Absolute stereochemistry.
Double bond geometry as shown.



≠ Comp.

CM 2

CRN 76-05-1
CMF C2 H F3 O2



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:754159 CAPLUS
DN 137:263297
TI Preparation of 2,7-diamino-5-heptenoic acid derivatives for the treatment of cancer
IN Manning, Pamela T.; Connor, Jane R.; Seibert, Karen; Rao, Chinthalapally

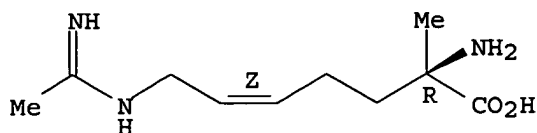
10/646266

V.; Reddy, Bandaru S.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 295 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|--|----------|-----------------|----------|
| PI | WO 2002076395 | A2 | 20021003 | WO 2002-US8938 | 20020321 |
| | WO 2002076395 | A3 | 20040812 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | US 2003013702 | A1 | 20030116 | US 2001-961969 | 20010924 |
| | EP 1463495 | A2 | 20041006 | EP 2002-717708 | 20020321 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| | JP 2005500259 | T2 | 20050106 | JP 2002-574911 | 20020321 |
| PRAI | US 2001-278512P | P | 20010323 | | |
| | US 2001-961969 | A | 20010924 | | |
| | WO 2002-US8938 | W | 20020321 | | |
| OS | MARPAT 137:263297 | | | | |
| AB | Agents and methods for chemoprevention and treatment of neoplasia are described, the agents including a selective inhibitor of inducible nitric oxide synthase and a combination of a selective inhibitor of inducible nitric oxide synthase and an inhibitor of cyclooxygenase-2 in a pharmaceutical composition 2,7-Diamino-5-heptenoic acid derivs. R7N:CMenHCH2CR1:CR2CH2CH2CH(NH2)C(O)J [R1, R2 = H, halo, alkyl, haloalkyl (at least one of R1 or R2 contains halogen); R7 = H, OH; J = OH, alkoxy, NR3R4, where R3 = H, alkyl, alkenyl, alkynyl and R4 = H, (un)substituted heterocyclyl] or their pharmaceutically-acceptable salts are among the compds. claimed. Thus, (2S,5E)-2-amino-6-fluoro-7-[(1-iminoethyl)amino]-5-heptenoic acid dihydrochloride was prepared by a multistep procedure starting from L-glutamic acid and showed IC50 values 0.36, 68, 3.6, and 0.1 µM in hiNOS, hecNOS, hncNOS, and human cartilage assays, resp. | | | | |
| IT | 404385-53-1P | | | | |
| | RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of diaminoheptenoic acid derivs. for treatment of cancer) | | | | |
| RN | 404385-53-1 | CAPLUS | | | |
| CN | 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2R,5Z)- (9CI) (CA INDEX NAME) | | | | |

Absolute stereochemistry.
Double bond geometry as shown.

10/646266



Comp.

● 2 HCl

L3 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:220540 CAPLUS
 DN 136:263465
 TI Preparation of 2-amino-2-alkyl-5-heptenoic and -heptynoic acid derivatives
 useful as nitric oxide synthase inhibitors
 IN Hansen, Donald, Jr.; Webber, Ronald Keith; Pitzele, Barnett S.; Sikorski,
 James; Massa, Mark A.; Hagen, Timothy J.; Grapperhaus, Margaret; Wang,
 Lijuan Jane; Bergmanis, Arija A.; Kramer, Steven W.; Hallinan, E. Ann
 PA Pharmacia Corporation, USA
 SO PCT Int. Appl., 216 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2002022562 | A1 | 20020321 | WO 2001-US28673 | 20010915 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2421504 | AA | 20020321 | CA 2001-2421504 | 20010915 |
| AU 2001090883 | A5 | 20020326 | AU 2001-90883 | 20010915 |
| US 2002132849 | A1 | 20020919 | US 2001-953049 | 20010915 |
| EP 1317421 | A1 | 20030611 | EP 2001-970937 | 20010915 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001013925 | A | 20030701 | BR 2001-13925 | 20010915 |
| JP 2004509099 | T2 | 20040325 | JP 2002-526762 | 20010915 |
| ZA 2003001575 | A | 20040226 | ZA 2003-1575 | 20030226 |
| NO 2003001140 | A | 20030508 | NO 2003-1140 | 20030312 |
| PRAI US 2000-232683P | P | 20000915 | | |
| WO 2001-US28673 | W | 20010915 | | |
| OS MARPAT 136:263465 | | | | |
| AB 2-Amino-2-alkyl-5-heptenoic acids derivs. HN:CM ₂ NHCH ₂ CR ₃ :CR ₂ CH ₂ CH ₂ CR ₁ (NH ₂)CO ₂ H (R ₁ = alkyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl; R ₂ , R ₃ = H, halo or any group given for R ₁) and corresponding heptynoic derivs. HN:CM ₂ NHCH ₂ C.tplbond.CCH ₂ CH ₂ CR ₁ (NH ₂)CO ₂ H were prepared as nitric oxide synthase (NOS) inhibitors. Thus, (2S/5E)-2-amino-2-methyl-6-fluoro-7-[(1-iminoethyl)amino]-5-heptenoic acid dihydrochloride was prepared by a multistep procedure starting with the reaction of tri-Et 2-fluorophosphonoacetate with 3-[(tert-butyldimethylsilyl)oxy]propanal and showed IC ₅₀ = 0.4, 37, and 7.6 μM for inhibition of hNOS, hecNOS, and hncNOS, resp. | | | | |
| IT 404385-39-3P 404385-53-1P 404385-91-7P | | | | |

10/646266

404386-04-5P 404386-20-5P 404386-33-0P

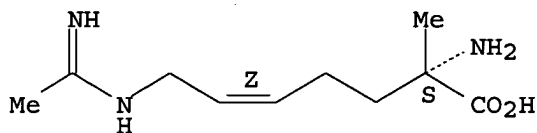
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminoalkylheptenoic and -heptynoic acid derivs. useful as nitric oxide synthase inhibitors)

RN 404385-39-3 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



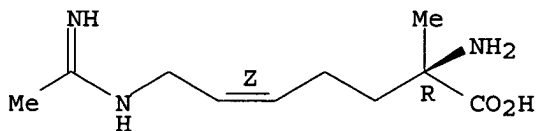
F Comp

● 2 HCl

RN 404385-53-1 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, dihydrochloride, (2R,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



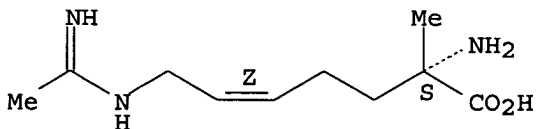
F Comp

● 2 HCl

RN 404385-91-7 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



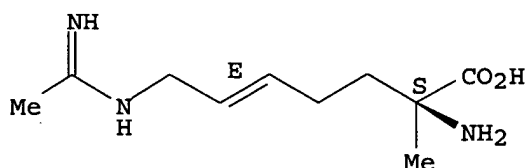
F Comp

RN 404386-04-5 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2S,5E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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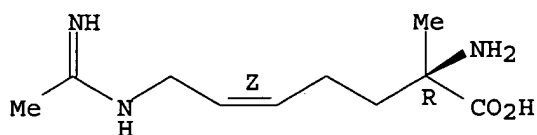


F Conf

RN 404386-20-5 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2R,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

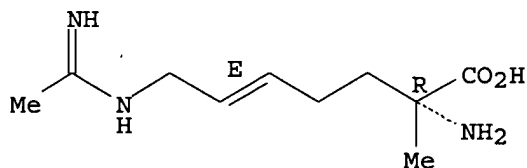


F Conf

RN 404386-33-0 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, (2R,5E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



F Conf

IT 404385-44-0P

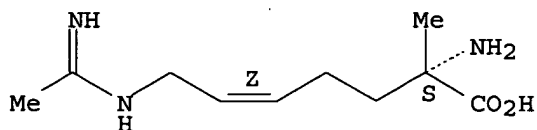
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aminoalkylheptenoic and -heptynoic acid derivs. useful as nitric oxide synthase inhibitors)

RN 404385-44-0 CAPLUS

CN 5-Heptenoic acid, 2-amino-7-[(1-iminoethyl)amino]-2-methyl-, monohydrochloride, (2S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



F Conf

● HCl

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

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ALL CITATIONS AVAILABLE IN THE RE FORMAT